1. Information Disclosure Statement

The Official Action states in the relevant part that:

> The information disclosure statement (IDS) filed on 25 February 2005 and 18 March 2005 fail to comply with 37 CFR 1.97, 1.98 and MPEP §609, which require a concise explanation of relevance or English-language translation of any non-English language documents cited on the IDS. The IDS lists both English and non-English documents. Although all documents have been placed in the application file, only those documents in English have been considered.

Applicants respectfully submit an Information Disclosure Statement, along with this response, for the English-language translation of a part of JP 04-368323 A of which the English-language abstract was filed on February 25, 2005. A partial English-language translation of this document is attached. Accordingly, the Examiner is respectfully requested to consider the content of the art (JP 04-368323 A) in the examination of the pending claims.

2. Claim Rejection(s) - 35 U.S.C. §103(a)

The Official Action states in the relevant part that claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,495,159 to Hirano et al. in view of US 2004/0028724 A1 to Terahara et al.

As the basis of the rejection, the Official Action states in relevant part:

> ...Examples 1, 6 and 8 in US '159 disclose an adhesive preparation that comprises a drug, styrene-isoprene-styrene block copolymer, 2-ethylhexyl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer. Polyisobutylene as exemplified in the examples

qualifies as basic-nitrogen including polymer having no adhesion property at normal temperature.

... The basic requirements of the invention as detailed in instant claim 1 are met with US '159. The selection of the specific nitrogen-including polymer appears to be a matter of preference. However, it was known at the time of invention per the art of US '157 (*Applicants assume this is an typological error of '159*) that polyvinyl acetal diethylamino acetate and methyl methacrylate-butyl methacrylate-dimethyl-aminoethyl methacrylate or polyvinyl acetal diethylamino acetate (commercially available as Eudragit E, Rohm GmbH) were effective nitrogen-including polymers in transdermal adhesives with specific utility in transdermal adhesives comprising styrene isoprene-styrene block copolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, see claims 1, 5 and 10 of US '724.

... Therefore, it would be reasonable to conclude that one of ordinary skill in the art at the time of the invention could modify the invention of '159 with the teachings of '724 to obtain the instant invention. The artisan would have been motivated to do so to obtain the specific therapeutic benefits of the drug being administered transdermally. The combined teachings of US '724 and '159 make prima facie obvious the instant application.

Applicants respectfully traverse this rejection.

The Examiner has failed to establish a *prima facie* case of obviousness against the presently rejected claims. To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the

background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, *supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

The presently pending claim 1, a single independent claim of the subject application, is directed to a patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with a drug and an adhesive base agent, wherein the adhesive base agent comprises styrene-isoprene-styrene block copolymer, 2-ethylheyxl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature.

By employing an adhesive base agent containing the aforementioned three components, i.e., styrene-isoprene-styrene block copolymer, 2-ethylheyxl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer including a basic nitrogen

and having no adhesion property at normal condition, the difficulty of achieving compatibility between the skin permeability of a drug and the patch properties has been overcome. Also, by compounding a drug with the adhesive base agent containing those three components in an adhesive layer, that is to say, by allowing the drug to coexist with the adhesive base agent, the solubility of a drug in the adhesive layer is enhanced, and the formation of a formulation could be conducted easily and surely. Further, since the drug could be compounded in the adhesive layer up to a supersaturated state without crystallization of the drug, the skin permeability of the drug could be enhanced (see, each 1st paragraph at page 3 and 4 of the specification).

In contrast, US 6,495,159 (hereinafter US '159), discloses a percutaneous therapeutic apparatus having a fundamentally different layer structure from the patch in the presently pending claims. As can be seen from Fig. 1 in US '159, the apparatus comprises a drug impermeable backing layer, a drug storage layer between the backing layer and a drug releasing layer containing a porous material of a drug permeable film, and a pressure-sensitive adhesive layer laminated to outer layer of the porous material. By employing such a layer structure, the US '159 apparatus prevents the drug from oozing from the apparatus and controls release of the drug to the skin. Accordingly, US '159 does not disclose a patch comprising an adhesive layer in which a drug coexists with an adhesive base agent comprises styrene-isoprene-styrene block copolymer, 2-ethylheyxl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature.

Further, US '159 does not disclose the "basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature".

The pressure-sensitive adhesive in US '159 makes use of preferably a pressure-sensitive adhesive comprising rubber elastomer, tackifier resin and softening agent, or a pressure-sensitive adhesive further containing acrylic type pressure-sensitive adhesive other than these three components. The "polyisobutylene" which the Examiner indicated in the Office Action at page 3 corresponded to the presently claimed basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature, is actually not a basic nitrogen-including polymer, but rather is an example of a rubber elastomer (see, column 5, lines 43-67 of US '159), formed as the homopolymer of 2-methyl-1-propene. As such, applicants respectfully submit that, contrary to the Examiner's allegation, none of Examples 1, 6 and 8 in US '159 discloses compositions of the pressure-sensitive adhesive which have a basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature. Accordingly, US '159 fails to discloses the basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal temperature element required by the presently pending claims.

Further, regarding presently pending claim 5, applicants respectfully assert that the dibutyl hydroxytoluene component of US '159 is a phenol compound and is not an organic acid as stated by the Examiner. Accordingly, contrary to the Examiner's assertions, US '159 does not meet the organic acid limitation of presently pending claim 5.

US 2004/0028724 (hereinafter US '724) does not remedy these deficiencies. US '724 discloses an adhesive pharmaceutical preparation comprising a polymer compound having amino groups at equal to or great than a certain amount (e.g., methyl

methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate copolymer), a drug forming an acid addition salt, and carboxylic acid and/or a salt thereof, and a rubber polymer (e.g., styrene-isoprene-styrene block copolymer), as can be seen in claim 10.

However, US '724 does not specifically disclose 2-ethylhexyl acrylate-vinyl acetate copolymer as one of components of the adhesive agent as in the presently pending claims; US '724 provides only general teachings of the possible layer structures of the adhesive pharmaceutical preparations (see, at page 4, [0041]-[0043]). Therefore, US '724 fails to disclose a patch comprising an adhesive layer in which a drug coexists with styrene-isoprene-styrene block copolymer, 2-ethylheyxl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal condition, as required by the presently pending claims.

As noted above, neither US '159 nor US '724, alone or in combination, teaches or discloses all of the limitations of presently pending independent claim 1. As mentioned above, US '159 discloses a patch having a different layer structure than that presently claimed and US '724 provides only general teachings of possible adhesive layers and the preparations thereof. Accordingly, the references cited by the Examiner, taken alone or in combination, do not disclose every element of the presently pending claims as required by *In re Wilson*.

In addition, there is **no** apparent reason to combine the elements of US '159 with the elements of US '724 in the fashion claimed by the presently pending claims. The percutaneous therapeutic apparatus containing at least three layers disclosed in US '159 is characterized by a separated layer structure, for a drug of (semi)liquid serotonin

receptor antagonist, where a drug storage layer containing a drug is provided between a backing layer and a drug releasing layer containing a pressure-sensitive layer which is able to control release of a drug from the apparatus. This is to prevent the drug from oozing, to reduce skin irritation and to control release of a drug. In contrast, the adhesive pharmaceutical preparation in US '724 contains a polymer compound having amino groups, for an acid addition salt of a basic drug or amphoteric drug. US '724 is directed to enhancing skin permeability of a drug in the form of a salt by converting it to the drug in a non-ionized form.

Accordingly, each of US '159 and US '724 teaches different technical tools and constitutions (improved layer structure vs. composition); neither of the references teaches nor suggests the presently claimed patch comprising an adhesive layer where a drug coexists with an adhesive agent of styrene-isoprene-styrene block copolymer, 2-ethylheyxl acrylate-vinyl acetate copolymer, and a basic nitrogen-including polymer including a basic nitrogen and having no adhesion property at normal condition.

Further, applicants again respectfully point out that US '159 does not in fact disclose a basic nitrogen-including polymer, since polyisobutylene is a homopolymer of 2-methyl-1-propene and does not contain any nitrogen atoms. As such, the Examiner's indication that "The selection of the specific nitrogen-including polymer appears to be a matter of preference. However, it was know at the time of invention...that polyvinyl acetal diethylamino acetate and methyl methacrylate-butyl methacrylatge-dimethyl-aminoethyl methacrylate or polyvinyl acetal diethylamino acetate (commercially available as Eudragit E, Rohm GmbH) where effective nitrogen-including polymers" is simply not true. Contrary to the Examiner's assertions, since US '159 does not disclose

any nitrogen-including polymers, a person of ordinary skill in the art reading US '159 would have had absolutely no reason to select a specific nitrogen-including polymer to arrive at the presently pending claims.

Accordingly, applicants submit that there is no apparent reason that would have prompted one of ordinary skill in the art to combine the elements of US '159 and US '724 to arrive at the presently pending claims.

Furthermore, a person of ordinary skill in the art would have had **no** reasonable expectation of success in combining US '159 and US '724 to reach the presently pending claims. In view of the general teachings in US '159 of the possible preparation forms and in view of the specific teachings in US '724 to the patch layer structure, one of ordinary skill in the art would only potentially have reached the patch in US '159 having a different composition in the pressure-sensitive adhesive layer than that presently claimed.

As such, US '159 and US '724, taken alone or in combination, do not teach, disclose, or render obvious the presently pending independent claim 1 and its dependent claims 2-6. Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of presently pending claims 1-6.

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is believed to be patentably distinguishable over the prior art of record. The Examiner is respectfully requested to reconsider and withdraw the outstanding rejections and allow all pending claims 1-6. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,

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